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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S): Lo et al.

SERIAL NUMBER: Not Yet Assigned  
(Divisional of U.S.S.N. 09/575,503)

GROUP NUMBER: Not Yet Assigned

FILING DATE: October 11, 2001

EXAMINER: Not Yet Assigned

TITLE: EXPRESSION AND EXPORT OF INTERFERON-ALPHA PROTEINS  
AS Fc FUSION PROTEINS

Box PATENT APPLICATION

Commissioner for Patents

Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

Please enter this Preliminary Amendment for the above-identified divisional Application prior to calculating the filing fee. Claims 1-29 were subject to a restriction requirement in the co-pending parent U.S. Application Serial No. 09/575,503.

Applicants herein cancel claims 1-25 without prejudice and amend claims 26-27. Applicants add new claims 30-38. Accordingly, after entry of this Amendment, claims 26-38 will be pending for examination.

A petition for a three-month extension of time up to and including October 11, 2001, is filed today in the co-pending parent U.S. Application Serial No. 09/575, 503.

**In the Specification**

Please amend the following paragraph of the specification, identified by page and line number, to read as follows. A marked up version of the amended paragraph is attached at the end of this Preliminary Amendment.

Replacement Paragraph for the priority claim at page 1, lines 4-7

**Related Applications**

This Application is a divisional of U.S. Application Serial No. 09/575,503, filed May 19, 2000, which claims priority to U.S. Provisional Application Serial No. 60/134,895, filed May 19, 1999, the entire disclosures of which are incorporated herein by reference.

**In The Claims**

Please cancel claims 1-25 without prejudice. Please amend claims 26-27 and add new claims 30-38 as follows. A marked up version of the amended claims is attached at the end of this Preliminary Amendment.

26. (Amended) A method of treating a condition alleviated by the administration of interferon-alpha, the method comprising the step of administering to a mammal a fusion protein that binds an Fc receptor expressed on a target cell, wherein the fusion protein comprises in an N- to C-terminal direction an immunoglobulin Fc region and an interferon-alpha protein, thereby to treat a condition in said mammal.

27. (Amended) A method of treating a condition alleviated by the administration of interferon-alpha, the method comprising the step of administering to a mammal a multimeric protein comprising at least two fusion proteins, wherein the multimeric protein binds an Fc receptor expressed on a target cell, and wherein each fusion protein comprises in an N- to C-terminal direction an immunoglobulin Fc region and an interferon-alpha protein, thereby to treat a condition in said mammal.

30. (New) The method of claim 26, wherein the target cell is a liver cell.

31. (New) The method of claim 27, wherein the target cell is a liver cell.

32. (New) The method of claim 27, wherein the condition is a liver disorder.

33. (New) The method of claim 32, wherein the liver disorder is hepatitis.

34. (New) The method of claim 26, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region.
35. (New) The method of claim 26, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region and an immunoglobulin heavy chain constant region domain.
36. (New) The method of claim 30, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region and an immunoglobulin CH3 domain.
37. (New) The method of claim 27, wherein the multimeric protein comprises at least two fusion proteins that are linked via a covalent bond.
38. (New) The method of claim 26, wherein the fusion protein is encoded by a nucleic acid molecule comprising:
- (a) a signal sequence; (b) an immunoglobulin Fc region; and (c) an interferon-alpha sequence,
- wherein the signal sequence, the immunoglobulin Fc region and the interferon-alpha sequence are encoded serially in a 5' to 3' direction.

#### **REMARKS**

Applicants cancel originally filed claims 1-25 without prejudice. Applicants amend claims 26-27 and introduce new claims 30-38. Accordingly, after the entry of this Amendment, claims 26-38 will be pending for examination. Applicants submit that no new matter is introduced and that claims 26-38 are in condition for allowance.

#### **Amendments to the Specification**

The specification is amended to include a specific reference to an earlier filed Application the benefit of which is claimed herein under 35 U.S.C. § 120.

Accordingly, Applicants submit that no new matter is introduced.

Amendments to the Claims

Dependent claim 26 is rewritten as an independent claim. Support for this amendment is found in the application as filed at least on pages 6, lines 22-25; page 9, lines 5-7; and in the originally filed claim 11.

Dependent claim 27 is also rewritten as an independent claim. Support for this amendment is found in the application as filed at least on page 13, lines 3-8; and in the originally filed claim 18.

Applicants submit that no new matter is introduced by these amendments.

New Claims

New claims 30-38 are generally directed to a method of treating a condition alleviated by an interferon-alpha fusion protein.

Support for claim 30 is found in the application as filed at least on page 7, lines 3-5; and page 8, lines 24-25. Support for claim 31 is found in the application as filed at least on page 7, lines 3-5. Support for claim 32 is found in the application as filed at least on page 7, lines 5-8. Support for claim 33 is found in the application as filed at least on page 7, lines 5-8. Support for claim 34 is found in the application as filed at least on page 4, lines 17-18; and 11, lines 20-21. Support for claim 35 is found in the application as filed at least on page 4, lines 17-19; and page 11, lines 20-22. Support for claim 36 is found in the application as filed at least on page 4, lines 17-20; and page 11, lines 20-22. Support for claim 37 is found in the application as filed at least on page 13, lines 3-8. Support for claim 38 is found in the application as filed at least on page 6, lines 22-25; page 11, lines 3-5; and in the originally filed claim 1.

Accordingly, Applicants submit that no new matter is introduced by the new claims.

Declarations

Applicants submit herewith a copy of the originally filed Declaration (3 pages) that was filed in the prior parent application U.S. Serial No. 09/575,503.

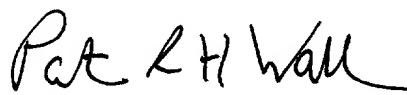
Sequence Listing

Applicants hereby state that the computer readable form of sequence listing in the instant divisional application, is identical with that filed in the co-pending parent Application Number 09/575,503, filed on May 19, 2000. Applicants submit paper copies of the sequence listing and a statement verifying the identity of the paper copy and the computer readable form which were filed in U.S.S.N. 09/575, 503. In accordance with 37 CFR 1.821 (e), Applicants request the use of the computer readable form of sequence listing filed in United States Serial Number 09/575,503.

CONCLUSION

Applicants respectfully submit that claims 26-38 are in condition for allowance and request entry as such. Applicants believe that no additional fees are necessitated by the present Amendment. However, in the event that any additional fees are due, the Director is hereby authorized to charge any such fees to Attorney's Deposit Account No. 20-0531. The Patent Office is invited to call the undersigned if it is believed that a telephone conversation could be helpful in expediting prosecution of this application.

Respectfully submitted,



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Date: October 11, 2000

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**MARKED UP VERSION OF SPECIFICATION SHOWING AMENDMENTS**

**Related Applications**

This application is a divisional of U.S. Application Serial No. 09/575,503, filed May 19, 2000, [This application] which claims priority to U.S. Provisional Application [Ser.] Serial No. 60/134,895, filed May 19, 1999, the entire disclosures of which are[is] incorporated herein by reference.

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**MARKED UP VERSION OF CLAIMS SHOWING AMENDMENTS**

26. (Amended) A method of treating a condition alleviated by the administration of interferon-alpha, the method comprising the step of administering to a mammal a fusion protein [of claim 11 to a mammal having the condition] that binds an Fc receptor expressed on a target cell, wherein the fusion protein comprises in an N- to C-terminal direction an immunoglobulin Fc region and an interferon-alpha protein, thereby to treat a condition in said mammal.
27. (Amended) A method of treating a condition alleviated by the administration of interferon-alpha, the method comprising the step of administering to a mammal [protein of claim 18 to a mammal having the condition] a multimeric protein comprising at least two fusion proteins, wherein the multimeric protein binds an Fc receptor expressed on a target cell, and wherein each fusion protein comprises in an N- to C-terminal direction an immunoglobulin Fc region and an interferon-alpha protein, thereby to treat a condition in said mammal.
- 30. (New) The method of claim 26, wherein the target cell is a liver cell.
31. (New) The method of claim 27, wherein the target cell is a liver cell.
32. (New) The method of claim 27, wherein the condition is a liver disorder.
33. (New) The method of claim 32, wherein the liver disorder is hepatitis.
34. (New) The method of claim 26, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region.

35. (New) The method of claim 26, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region and an immunoglobulin heavy chain constant region domain.
36. (New) The method of claim 30, wherein the immunoglobulin Fc region comprises an immunoglobulin hinge region and an immunoglobulin CH3 domain.
37. (New) The method of claim 27, wherein the multimeric protein comprises at least two fusion proteins that are linked via a covalent bond.
38. (New) The method of claim 26, wherein the fusion protein is encoded by a nucleic acid molecule comprising:
- (b) a signal sequence; (b) an immunoglobulin Fc region; and (c) an interferon-alpha sequence,
- wherein the signal sequence, the immunoglobulin Fc region and the interferon-alpha sequence are encoded serially in a 5' to 3' direction. --